ORM PTO-1	449/ A ar	nd B (Modif	ied)		ELICATION NO.: 09/824,468	ATTY.	DOCKET NO.: C01	1039/70049
SUPPL			FORMAÇI	PRADEMANT	LING DATE: April 2, 2002	CONFI	RMATION NO.: 904	46
STAT		SCLOSU NT BY A	JRE PPLICANT	S AI	PPLICANT: Krieg et al.			
heet 1		of	1	GI	ROUP ART UNIT: 1642 1635	EXAM	IINER: Unassigned	Gibb
					PATENT DOCUMENTS		·-	408
	Cite	U	.S. Patent Docu		Name of Patentee or Applicant of	of Cited	Date of Publicati	on or of issue
aminer's itials#	No.	1	Number	Kind Code	Document			cument YYYY
							חבר	FIVE
							MEL	0.0002
							SEP	
							TECH CE	NTER 1600
				FOREI	GN PATENT DOCUMENTS			
caminer's	Cite No.	Office/	eign Patent Doc	Kind	Name of Patentee or Applicant of Document (not necessary)	of Cited	Date of Publication of Cited Document MM-DD-YYYY	Translation (Y/N)
DI	B2 (Country CA	2,319,309	Code A1	SmithKline Beecham Biologicals	S.A.	08/03/00	Y
-								
						· ·		
				1				
					PATENT LITERATURE DOCUME			
kaminer's itials#	Cite No		ook, magazine,	journal, seria	TAL LETTERS) title of the article (wall, symposium, catalog, etc.), date, rellisher, city and/or country where pub	evant page(Translation (Y/N)
			1 - 19 27 20 77 4 - 11.					
	•					······································	10000	
-	6	un	()21 ()	<u> </u>	DATE CONSIDERED			
XAMINER			VI/I I /		i .	(1)	1. ~	

,,	OIP	THE YEAR OF THE PARTY OF THE PA					RECEN	/ED:
FORM (20)	1449/A a	nd Brylodified)		APPLICAT	ION NO.: 09/824,468	ATTY	DOCKET NO.: CI	039/7049
INF	STANCE N	TION DISCLOSUE	RE		TE: 04/02/2001		JUN 1 4 DOCKET NO.: CIP TECH CENTER	1600 2901
STA	TEME	NT BY APPLICAN			Γ: Krieg et al.			
Sheet	1	of 1		GROUP AR	T UNIT: Upknown	EXAM	INER: Unassigne	d,
					DOCUMENTS			
F	Cite	U.S. Patent Doc	ument	Nam	e of Patentee or Applicant of	Cited	Date of Publicati	on or of issue
Examiner's Initials#	No.	Number	Kind Code	i	Document		of Cited Do MM-DD-Y	
	A17	6,194,388	B1	Krieg e			02/27/2001	
J.A	A18	6,207,646	B1	Krieg 6	et al.		03/27/2001	
			FOR	REIGN PATE	NT DOCUMENTS			
Examiner's Initials#	Cite No.	Foreign Patent Do Office/ Number	Kind	1	e of Patentee or Applicant of Document (not necessary)	Cited	Date of Publication of Cited Document	Translation (Y/N)
		Country	Code				MM-DD-YYYY	
	-		-					**
		OTHE	R ART — N	ON PATENT	LITERATURE DOCUMEN	TS .		
Examiner's Initials#	Cite No	Include name of the au item (book, magazine	thor (in CA e, journal, se	PITAL LET erial, sympos	TERS) title of the article (whe ium, catalog, etc.), date, relevay and/or country where publis	en approp ant page(s	, .	Translation (Y/N)
					, <u>44-14-14-14-14-14-14-14-14-14-14-14-14-1</u>	* .	. , , , , , , , , , , , , , , , , , , ,	
	<u>.</u> l				110 thinks me one			
EXAMINE	Du	v JOQ			DATE CONSIDERED $6/26/03$	·		
	nitial if refe			in conformance	e with MPEP 609; Draw line throug	gh citation i	f not in conformance ar	d not considere
'a copy of this re	eference is n earlier fil	not provided as it was previous ing date under 35 U.S.C. 120 (sly cited by or continuation,	r submitted to the continuation-in	ne office in a prior application, Serin-part, and divisional applications).	al No	, filed	, a

TORINI 10-1447/A and D (Modified)					APPLICATION NO.: 09/824,468 ATTY.		ГҮ. DOCKET NO.: C01039/70049		
INFO	RMA	TĮON DI:	SCLOSURI PPLICANT	E FI	LING DATE: April 2, 2002	CONFI	RMATION NO.: 904	6	
STA	WME	NT BY A	PPLICANT	A	PPLICANT: Krieg et al.				
Sheet 🙀	APR 2 E	3002 E	1	G	ROUP ART UNIT: 1642 1635	EXAM	IINER: Unasøigne	وحكرا ٥	35
1 To	P PADI	Rt OF		U.S.	PATENT DOCUMENTS		(ji.	bbs	
Examiner's	Cite	T .	S. Patent Docu	ment	Name of Patentee or Applicant o	f Cited	Date of Publication		issue
nitials#	No.	N	lumber	Kind Code	Document		of Cited Do MM-DD-Y		
L	A19	2001003	6462	A1	Fong et al.		11/01/2001		
		-	·····			· · · · · · · · ·	DECE	<u> </u>	
					COPY OF PAPERS		RECE	VE	<u></u>
					ORIGINALLY FILED		APR 3	9-2002	
							TECH CENTER	1600/	290
]						1 LOIT OLITTLE	1000	
	T	1		FORE	IGN PATENT DOCUMENTS		Date of	·	
Examiner's initials#	Cite No.	Office/	eign Patent Doc Number	ument Kind Code	Name of Patentee or Applicant of Document (not necessary)	of Cited	Publication of Cited Document MM-DD-YYYY	Trans (Y/	slatio 7/N)
		Country		Code			NAME DE LA CASA		-
	\ -								
		l	<u> </u>		1		<u></u>	J	
Examiner's Initials#	Cite No	Include i	name of the aut	hor (in CAP journal, ser	N PATENT LITERATURE DOCUME ITAL LETTERS) title of the article (w ial, symposium, catalog, etc.), date, rel	hen appro	priate), title of the (s), volume-issue	Trans	slatio '/N)
			nu	ımber(s), pu	blisher, city and/or country where pub	lished.			T
· · · · · · · · · · · · · · · · · · ·	1								+-
						- 13-13-14-15-15-15-15-15-15-15-15-15-15-15-15-15-		<u> </u>	-
EXAMINE	\sim		200		DATE CONSIDERED	6/76/	, n 2	 	
		un x	7		conformance with MPEP 609; Draw line thro	1 20/1			

FORM PTO-1449(Modified)

LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.: C1039/7049 (HCL/MAT)

SERIAL NO.: not yet assigned

APPLICANT: Krieg, et al.

FILING DATE: Herewith

GROUP: 1635

U.S. PATENT DOCUMENTS

Exam Init	Ref Des	Document No.	Date	Name	Class	Sub Class	FILING DATES If Appropriates
70	*A1	3,906,092	09/16/75	Hilleman et al.	424	89 /	
	*A2	5,212,295	5/18/93	Cook	536	26.7	
	*A3	5,248,670	09/28/93	Draper et al.	514	44/	
	*A4	5,506,212	04/09/96	Hoke et al.	314	4/4	
	*A5	5,521,302	5/28/96	Cook	536	25.31	
П	*A6	5,585,479	12/17/96	Hoke et al.	536	∴ /2 4.5	
	*A7	5,599,797	02/04/97	Cook et al.	514	/ 44	
	*A8	5,663,153	09/02/97	Hutcherson et al.	514	44	
	*A9	5,723,335	03/03/98	Hutcherson et al.	435	375	
	*A10	5,750,674	05/12/98	Iyer et al.	536/	26.7	
	*A11	5,786,189	07/28/98	Locht et al.	435	72.3	
	*A12	5,837,856	11/17/98	Arnold, Jr. et al.	5 3 6	24.5	
	*A13	5,849,719	12/15/98	Carson et al.	5 14	44	
	*A14	5,856,465	01/05/99	Stec et al	536	25.8	
7.	*A15	5,883,237	03/16/99	Stec et al.	536	23.1	
RE	*A16	5,908,845	06/01/99	Segev	7 514	261	
	.1	l	1				

FOREIGN PATENT DOCUMENTS

_								
			Country & Doc. No. (11)	Pub. Date (43)		Class	Sub Class	Translation Yes No
7	Qf-	*B1	WO 91/12811	09/05/91	PCT	A61K	31/70	
	-	*B2	0468520 A3	01/29/92	EPO	A61K	31/79	
	1	*B3	WO 92/03456	03/05/92	PCT	ф07Н	15/1/2	
		*B4	WO 92/18522	10/29/92	PCT	С07Н	21/00	
		*B5	WO 92/21353	12/10/92	PCT	A6K	3/70	
		*B6	0302758 B1	03/16/94	EPO	C12N	5/37	
		*B7	WO 94/19945	09/15/94	PCT	A01N	43/04	
\square		*B8	WO 95/05853	03/02/95	Regents of the University of CA	C07H	21/00	
П		*B9	WO 95/26204	10/95	PCT	A61K	48/00	
П		*B10	WO 96/02555A1	02/01/96	University of Iowa	C120	1/68	
		*B11	WO 96/19572	06/27/96	Hybridon, Inc.	C07/H	1/04	
		*B12	WO 96/39154	12/12/96	Cook et al.	С07Н	2/00	
		*B13	WO 96/35782	11/14/96	Applied Research Systems	A/61K	48)00	
П		*B14	WO 97/28259	08/07/97	PCT	¢12N	15/00	
	^	*B15	WO 98/18810	05/07/98	University of Iowa	C07H	21/00	
T.	X	*B16	WO 98/37919	09/03/98	PCT	A61K	49/00	
∇	_							

524727.1524727.1

Fun Ho

6/24/03

L 2	*B17	WO 98/40100	09/17/98	PCT	A61K 39/39
	*B18	WO 98/52581	11/26/98	PCT	A6N 35/00
J	*B19	WO 98/14210	04/09/98	PCT	A61K 39/35
18	*B20	WO 00/06588	02/10/99	PCT	A61K 3170

		OTHER ART (Including Author, Title, Date, Pertinent Pages, Publication, Etc.)
Pa	*C1	Weiner, et al., "Immunostimulatory oligodeoxynucleotides containing the CpG motif are effective as immune
371	1.00	adjuvants in tumor antigen immunization"" Proc. Natl. Acad. Sci., (1997), 94:10833-10837
	*C2	Chu, et al., "CpG Oligodeoxynucleotides Act as Adjuvants that Switch on T Helper 1 (Th1) Immunity", J. Exp. Med., (1997), 186:10:1623-1631
	*C36	Liu, et al., "Immunostimulatory CpG Oligodeoxynucleotides Enhance the Immune Response to Vaccine Strategies Involving Granulocyte-Macrophage Cology-Stimulating Factor, <i>Blood</i> , (1998) 92:10:3730-3736
	*C4	Davis, H., et al., "CpG DNA is a Potent Enhancer of Specific Immunity in Mice Immunized with Recombinant Hepatitis B Surface Antigen", J of Immunol., (1998), 160:2:870-876
	*C1	Adya N et al., Expansion of CREB's DNA recognition specificity by Tax results from interaction with Ala-Ala-Arg at positions 282-284 near the conserved DNA-binding domain of CREB. <i>Proc Natl Acad Sci USA</i> 91(12):5642-6, 7 Jun 1994.
	*C2	Angier, N., Microbe DNA Seen as Alien By Immune System, New York Times, 4/11/95
	*C3	Azad RF et al., Antiviral Activity of a Phosphorothioate Oligonucleotide Complementary to RNA of the Human Cytomegalovirus Major Immediate-Early Region. <i>Antimicrobial Agents and Chemotherapy</i> , 37:1945-1954, September, 1993.
	*C4	Azuma, Biochemical and Immunological Studies on Cellular Components of Tubercle Bacilli, <i>Kekkaku</i> , Vol. 69, 9:45-55, 1992.
	*C5	Ballas ZK et al., Induction of NK activity in murine and human cells by CpG motifs in oligodeoxynucleotides and bacterial DNA. <i>J Immunol</i> 157(5):1840-5, 1996.
	*C6	Bayever, E., Systemic Administration of a Phosphorothioate Oligonucleotide with a Sequence Complementary to p53 for Acute Myelogenous leukemia and Myelodysplastic Syndrome: Initial Results of a Phase I Trial, <i>Antisense Res. & Dev.</i> (1993), 3:383-390.
EACTA	*C7	Bennett RM et al., DNA binding to human leukocytes. Evidence for a receptor-mediated association, internalization, and degradation of DNA. <i>J Clin Invest</i> 76(6):2182-90, 1985.
	*C8	Berg DJ et al., Interleukin-10 is a central regulator of the response to LPS in murine models of endotoxic shock and the Shwartzman reaction but not endotoxin tolerance. <i>J Clin Invest</i> 96(5):2339-47, 1995.
	*C9	Blanchard DK et al., Interferon-gamma induction by lipopolysaccharide: dependence on interleukin 2 and macrophages. <i>J Immunol</i> 136(3):963-70, 1986.
	*C10	Blaxter et al., Genes expressed in Brugia malayi infective third stage larvae. Molecular and Biochemical Parasitology, 77:77-93.
	*C11	Boggs RT et al., Characterization and modulation of immune stimulation by modified oligonucleotides. Antisense Nucleic Acid Drug Dev 7(5):461-71, Oct 1997.
	*C12	Branda RF et al., Amplification of antibody production by phosphorothioate oligodeoxynucleotides. <i>J. Lab Clin Med</i> 128(3):329-38, Sep 1996.
	*C13	Branda et al., Immune Stimulation by an Antisense Oligomer Complementary to the rev gene of HIV-1. Biochemical Pharmacology, Vol. 45, 10:2037-2043, 1993.
	*C14	Briskin M et al., Lipopolysaccharide-unresponsive mutant pre-B-cell lines blocked in NF-kappa B activation. Mol Cell Biol 10(1):422-5, Jan 1990.
	*C15	Chace, J. et al., Regulation of Differentiation in CD5+ and Conventional B Cells, Clinical Immunology and Immunopathology, (1993), 68:3:327-332.
	*C16	Chang YN et al., The palindromic series I repeats in the simian cytomegalovirus major immediate-early promoter behave as both strong basal enhancers and cyclic AMP response elements. <i>J Virol</i> 64(1):264-77, Jan 1990.
	*C17	Chu RS et al., CpG oligodeoxynucleotides act as adjuvants that switch on T helper 1 (Th1) immunity. J Exp Med 186(10):1623-31, 17 Nov 1997.
28	*C18	Cowdery JS et al., Bacterial DNA induces NK cells to produce IFN-gamma in vivo and increases the toxicity of lipopolysaccharides. <i>I Immunol</i> 156(12):4570.5, 15 Jun 1996

of lipopolysaccharides. J Immunol 156(12):4570-5, 15 Jun 1996.

Lk	*C19	Crosby et al., The Early Responses Gene FGFI-C Encodes a Zinc Finger Transcriptional Activator and is a Member of the GCGGGGGCG (GSG) Element-Binding Protein Family. <i>Mol. Cell. Biol.</i> , 2:3835-3841, 1991.
Acco	*C20	Crystal, Transfer of Genes to Humans: Early Lessons and Obstacles to Success. <i>Science</i> , Vol. 270, pp. 404-410, 1995.
	*C21	D'Andrea A et al., Interleukin 10 (IL-10) inhibits human lymphocyte interferon gamma-production by suppressing natural killer cell stimulatory factor/IL-12 synthesis in accessory cells. <i>J Exp Med</i> 178(3):1041-8, 1993.
	*C22	Englisch et al., Chemically Modified Oligonucleotides as Probes and Inhibitors, Angew. Chem. Int. Ed. Engl., 30:613-629, 1991.
	*C23	Erb KJ et al., Infection of mice with Mycobacterium bovis-Bacillus Calmette-Guerin (BCG) suppresses allergen- induced airway eosinophilia. <i>J Exp Med</i> 187(4):561-9, 16 Feb 1998.
	*C24	Etlinger, Carrier sequence selection - one key to successful vaccines, <i>Immunology Today</i> , Vol. 13, 2:52-55, 1992.
	*C25	Fox RI, Mechanism of action of hydroxychloroquine as an antirheumatic drug. <i>Chemical Abstracts</i> , 120:15, Abstract No. 182630 (April 29, 1994).
	*C26	Gao, W-Y et al., Phosphorothioate oligonucleotides are inhibitors of human DNA polymerases and Rnase H: Implications for antisense technology. <i>Mol. Pharmacol.</i> (1992), 41, 223-229.
	*C27	Gura, T., Antisense Has Growing Pains. Science (1995), 270:575-576.
	*C28	Hadden J et al., Immunostimulants. TIPS, (1993), 141:169-174.
	*C29	Hadden J et al., Immunopharmacology, JAMA, (1992) 268:20:2964-2969.
	*C30	Halpern MD et al., Bacterial DNA induces murine interferon-gamma production by stimulation of interleukin-12 and tumor necrosis factor-alpha. <i>Cell Immunol</i> 167(1):72-8, 1996.
	*C31	Hatzfeld J., Release of Early Human Hematopoietic Progenitors from Quiescence by Antisense Transforming Growth Factor 1 or Rb Oligonucleotides, J. Exp. Med., (1991) 174:925-929.
	*C32	Highfield PE, Sepsis: the More, the Murkier. Biotechnology, 12:828, August 12, 1994.
	*C33	Hoeffler JP et al., Identification of multiple nuclear factors that interact with cyclic adenosine 3',5'-monophosphate response element-binding protein and activating transcription factor-2 by protein-protein interactions. <i>Mol Endocrinol</i> 5(2):256-66, Feb 1991.
	*C34	Horspool JH et al., Nucleic acid vaccine-induced immune responses require CD28 costimulation and are regulated by CTLA4. <i>J. Immunol</i> , 160, 2706-2714, 1998.
	*C35	Iguchi-Ariga SM and Shaffner W, CpG methylation of the cAMP-responsive enhancer/promoter sequence TGACGTCA abolishes specific factor binding as well as transcriptional activation. <i>Genes Dev</i> 3(5):612-9, May 1989.
	*C36	Iverson, P., et al., "Pharmacokinetics of an Antisense Phosphorothioate Oligodeoxynucleotide against reve from Human Immunodeficiency Virus Type 1 in the Adult male Rate Following Single Injections and Continuous Infusion", <i>Antisense Research and Development</i> , (1994), 4:43-52
	*C37	Ishikawa R et al., IFN induction and associated changes in splenic leukocyte distribution. <i>J Immunol</i> 150(9):3713-27, 1 May 1993
	*C38	Jakway JP et al., Growth regulation of the B lymphoma cell line WEHI-231 by anti-immunoglobulin, lipopolysaccharide, and other bacterial products. <i>J Immunol</i> 137(7):2225-31, 1 Oct 1986.
	*C39	Jones TR et al., Synthetic oligonucleotides containing CpG motifs enhance immunogenicity of a peptide malaria vaccine in Aotus monkeys. <i>Vaccine</i> 17, 3065-3071 1999.
	*C40	Jaroszewski JW and Cohen JS, Cellular uptake of antisense oligonucleotides. Adv Drug Delivery Rev 6(3):235-50, 1991.
	*C41	Kimura Y et al., Binding of Oligoguanylate to Scavenger Receptors Is Required for Oligonucleotides to Augment NK Cell Activity and Induce IFN, J. Biochem., Vol. 116, 5:991-994, 1994.
	*C42	Kline JN et al., CpG motif oligonucleotides are effective in prevention of eosinophilic inflammation in a murine model of asthma. <i>J Invest Med</i> 44(7):380A, 1996.
\	*C43	Kline JN et al., Immune redirection by CpG oligonucleotides. Conversion of a Th2 response to a Th1 response in a murine model of asthma. <i>J Invest Med</i> 45(3):282A, 1997.
Ply	*C44	Kline JN et al., CpG oligonucleotides can reverse as well as prevent Th2-mediated inflammation in a murine model of asthma. <i>J Invest Med</i> 45(7):298A, 1997.

Lu HOL

6/26/03

4.0	*C45	Klinman DM et al., CpG motifs present in bacteria DNA rapidly induce lymphocytes to secrete interleukin 6, interleukin 12, and interferon gamma. Proc. Natl. Acad. Sci. USA 2027, 20
\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	*C46	interleukin 12, and interferon gamma. <i>Proc Natl Acad Sci USA</i> 93(7):2879-83, 1996. Krieg AM, An innate immune defense mechanism based on the recognition of CpG motifs in microbial DNA
	*C47	J Lab Clin Med 128(2):128-33, 1996. Krieg AM et al., Uptake of oligodeoxyribonucleotides by lymphoid cells is heterogeneous and inducible.
		Antisense Res Dev 1(2):161-71, Summer 1991.
	*C48	Krieg AM et al., Oligodeoxynucleotide modifications determine the magnitude of B cell stimulation by CpG
\vdash	*C49	motifs. Antisense Nucleic Acid Drug Dev 6(2):133-9, Summer 1996.
		Krieg AM et al., "Modification of antisense phosphodiester oligodeoxynucleotides by a 5' cholesteryl moiety increases cellular association and improves efficacy", <i>Proc. Natl. Acad. Sci.</i> , (1993), 90:1048-1052
	*C50	Krieg AM et al., "CpG DNA: A Pathogenic Factor in Systemic Lupus Erythematosus?", <i>Journal of Clinical Immunology</i> , (1995) 15:6:284-292
	*C51	Krieg AM et al, "Phosphorothioate Oligodeoxynucleotides: Antisense or Anti-Protein?, Antisense Research and Development, (1995), 5:241
	*C52	Krieg AM et al., "Leukocyte Stimulation by Oligodeoxynucleotides", Applied Antisense Oligonucleotide Technology, (1998), 431-448
	*C53	Krieg AM et al., CpG motifs in bacterial DNA trigger direct B-cell activation. Nature 374:546-9, 1995.
	*C54	Krieg AM et al, "The role of CpG dinuleotides in DNA vaccines", Trends in Microbiology, Vol. 6, pp. 23 27, Jan 1998.
	*C55	Krieg AM el al, "A Role for Endogenous Retroviral Sequences in the Regulation of Lymphocyte Activation, the Journal of Immunology, Vol. 143, 2448-2451,
	*C56	Kuramoto et al., Oligonucleotide Sequences Required for Natural Killer Cell Activation, <i>Jpn. J. Cancer Res.</i> 83:1128-1131, November 1992.
	*C57	Leonard et al., Conformation of Guanine 8-Oxoadenine Base Pairs in the Crystal Structure of d(CGCGAATT(08A)GCG). <i>Biochemistry</i> , 31(36):8415-8420, 1992.
	*C58	Macfarlane DE and Manzel L, Antagonism of immunostimulatory CpG-oligodeoxynucleotides by quinacrine, chloroquine, and structurally related compounds. <i>J Immunol</i> 160(3):1122-31, Feb 1 1998.
	*C59	Mastrangelo et al. Seminars in Oncology. Vol. 23, 1:4-21, 1996.
	*C60	Matson S and Krieg AM, Nonspecific suppression of [3H]thymidine incorporation by "control" oligonucleotides. <i>Antisense Res Dev</i> 2(4):325-30, Winter 1992.
	*C61	Manzel.L and Macfarlane, DE, Lack of Immune Stimulation by Immobilized CpG-Oligonucleotide. Antisense & Nucleic Acid Drug Development, 459-464, 1999
:	*C62	McIntyre KW et al., A sense phosphorothioate oligonucleotide directed to the initiation codon of transcription factor NF-kappa B p65 causes sequence-specific immune stimulation. <i>Antisense Res Dev</i> 3(4):309-22, Winter 1993.
	*C63	Messina et al., The Influence of DNA Structure on the <i>in vitro</i> Stimulation of Murine Lymphocytes by Natural And Synthetic Polynucleotide Antigens. <i>Cellular Immunology</i> , 147:148-157, 1993.
	*C64	Messina et al., Stimulation of <i>in vitro</i> Murine Lymphocyte Proliferation by Bacterial DNA. <i>J. Immunol.</i> , Vo. 147, 6:1759-1764, September 15, 1991.
'	*C65	Mojcik, C., et al., "Administration of a Phosphorothioate Oligonucleotide Antisense Murine Endogenous Retroviral MCF env Causes Immune Effect in vivo in a Sequence-Specific Manner", Clinical Immunology an Immunopathology, (1993), 67:2:130-136
	*C66	Mottram et al., A novel CDC2-related protein kinase from leishmania mexicana LmmCRK1 is post-translationally regulated during the life cycle. <i>J. Biol. Chem.</i> 268:28, 21044-21052 (October 1993).
-	*C67	New England BIOLABS 1988-1989 Catalog
'	*C68	Nyce JW and Metzger WJ, DNA antisense therapy for asthma in an animal model. <i>Nature</i> 385:721-725, 20 Feb 1997.
,	*C69	Pisetsky, D., "Stimulation of in vitro proliferation of murine lymphocytes by synthetic oligodeoxynucleotides", <i>Molecular Biology Repairs</i> , (1993) 18:217-221
	*C70	Pisetsky et al., Stimulation of Murine Lymphocyte Proliferation by a Phosphorothioate Oligonucleotide with Antisense Activity for Herpes Simplex Virus. <i>Life Science</i> , Vol. 54, pp. 101-107 (1994).
		Pisetsky, The Immunological Properties of DNA, The Journal of Immunology, pp. 421-423 (1996).
9/	C72	Pisetsky, Immunological Consequences of Nucleic Acid Therapy, Antisense Research and Development, 5:219-225 (1995).
27.1	. /	ne Jal 6/26/03

200	*C73	Raz E et al., Preferential induction of a Th1 immune response and inhibition of specific IgE antibody
IKN	*C74	formation by plasmid DNA immunization. <i>Proc Natl Acad Sci USA</i> 93(10):5141-5, 14 May 1996. Roman M et al., Immunostimulatory DNA sequences function as T helper-1-promoting adjuvants. <i>Nat Med</i>
	*C75	3(8):849-54, Aug 1997. Sato et al., Immunostimulatory DNA Sequences Necessary for Effective Intradermal Gene Immunization, Science, Vol. 273, pp. 352-354, 1996.
	*C76	Schnell et al., Identification and characterization of a Saccharomyces cerevisiae gene (PAR1) conferring resistance to iron chelators. <i>Eur. J. Biochem.</i> , 200:487-493.
	*C77	Schwartz DA et al., Endotoxin responsiveness and grain dust-induced inflammation in the lower respiratory tract. Am J Physiol 267(5 Pt 1):L609-17, 1994.
	*C78	Schwartz DA et al., The role of endotoxin in grain dust-induced lung disease. Am J Respir Crit Care Med 152(2):603-8, 1995.
	*C79	Schwartz DA et al., CpG motifs in bacterial DNA cause inflammation in the lower respiratory tract. <i>J Clin Invest</i> 100(1):68-73, 1 Jul 1997.
	*C80	Shirakawa T et al., The inverse association between tuberculin responses and atopic disorder. <i>Science</i> 275(5296):77-9, 3 Jan 1997.
	*C81	Sparwasser T et al., Macrophages sense pathogens via DNA motifs: induction of tumor necrosis factor-alpha-mediated shock. <i>Eur J Immunol</i> 27(7):1671-9, Jul 1997.
	*C82	Stein CA et al., Oligonucleotides as inhibitors of gene expression: a review. Cancer Research, 48:2659-2668 1988.
	*C83	Stull et al., Antigene, Ribozyme, and Aptamer Nucleic Acid Drugs: Progress and Prospects, <i>Pharmaceutical Res.</i> , Vol. 12, 4:465-483, 1995.
	*C84	Subramanian et al., Theoretical Considerations on the "Spine of Hydration" in the Minor Groove of d(CGCGAATTCGCG) d(GCGCTTAAGCGC): Monte Carlo Computer Simulation. <i>Proc. Nat'l. Acad. Sci. USA</i> , 85:1836-1840, 1988.
	*C85	Tanaka T et al., An antisense Oligonucleotide complementary to a sequence in IG2b increases G2b germline transcripts stimulates B cell DNA synthesis and inhibits immunoglobulin secretion. <i>J. Exp. Med.</i> , 175:597-607, 1992.
	*C86	Thorne PS., Experimental grain dust atmospheres generated by wet and dry aerosolization techniques. Am J Ind Med 25(1):109-12, 1994.
	*C87	Tokunaga T et al., Synthetic Oligonucleotides with Particular Base Sequences form the cDNA Encoding Proteins of <i>Myobacterium bovis</i> BCG Induce Interferons and Activate Natural Killer Cells, <i>Microbiol. Immunol.</i> , Vol. 36, 1:55-66, 1992.
	*C88	Tokunaga et al., A Synthetic Single-Stranded DNA, Ply (dG, dC), Induces Interferon / and -, Augments Natural Killer Activity and Suppresses Tumor Growth. <i>Jpn. J. Cancer Res.</i> , 79:682-686, June 1988.
	*C89	Uhlmann et al., Antisense Oligonucleotides: A New Therapeutic Principle. <i>Chemical Reviews</i> , 90:543-584, 1990.
	*C90	Wagner RW, Gene inhibition using antisense oligodeoxynucleotides. Nature, 372:L333-335, 1994.
	*C91	Wallace et al., Oligonucleotide probes for the screening of recombinant DNA libraries. <i>Methods in Enzymology</i> , 152:432-442 (1987).
	*C92	Weiss R., Upping the Antisense Ante: Scientists bet on profits from reverse genetics. Science, 139:108-109, 1991.
	*C93	Whalen R, DNA Vaccines for Emerging Infection Diseases: What If?, Emerging Infectious Disease, Vol. 2, 3:168-175, 1996.
	*C94	Wooldridge, JE et al., Immunostimulatory oligodeoxynucleotides containing CpG motifs enhance the efficacy of monoclonal antibody therapy of lymphoma. <i>Blood</i> , 89:2994-2998, 1997.
	*C95	Wu GY et al., Receptor-mediated gene delivery and expression in vivo. J. Biol. Chem., 263:14621-14624, 1988.
	*C96	Wu-Pong S., Oligonucleotides: Opportunities for Drug Therapy and Research. <i>Pharmaceutical Technology</i> , 18:102-114, 1994.
	*C97	Yamamoto S et al., DNA from bacteria, but not from vertebrates, induces interferons, activates natural killer cells and inhibits tumor growth. <i>Microbiol Immunol</i> 36(9):983-97, 1992.
28	*C98	Yamamoto S et al., <i>In vitro</i> augmentation of natural killer cell activity and production of interferon-alpha/beta and -gamma with deoxyribonucleic acid fraction from <i>Mycobacterium bovis</i> BCG. <i>Jpn J Cancer Res</i> 79:866-73, Jul 1988.
4727.1		Dun \$200 6(26/03

		*C99	Yamamoto S., Mode of Action of Oligonucleotide Fraction Extracted from Mycobacterium bovis BCG,					
VQ	\mathcal{L}	.033						
4			Kekkaku, Vol. 69, 9:29-32, 1994.					
1		*C100	Yamamoto S et al., Unique Palindromic Sequences in Synthetic Oligonucleotides are Required to Induce INF					
Ш			and Augment INF-Mediated Natural Killer Activity. J. Immunol., Vol. 148, 12:4072-4076, June 15, 1992.					
1 1		*C101	Yamamoto T et al., Ability of Oligonucleotides with Certain Palindromes to Induce Interferon Production and					
\			Augment Natural Killer Cell Activity is Associated with Their Base Length. Antisense Res. and Devel.,					
			4:119-123, 1994.					
		*C102	Yamamoto et al., Lipofection of Synthetic Oligodeoxyribonucleotide Having a Palindromic Sequence					
1	l		AACGTT to Murine Splenocytes Enhances Interferon Production and Natural Killer Activity. <i>Microbiol</i> .					
			Immunol., Vol. 38, 10:831-836, 1994.					
		*C103	Yamamoto T et al., Synthetic Oligonucleotides with Certain Palindromes Stimulate Interferon Production of					
			Human Peripheral Blood Lymphocytes in vitro. Jpn. J. Cancer Res., 85:775-779, 1994.					
		*C104	Yi, Ae-Kyung et al., IFN-y Promotes IL-6 and IgM Secretion in Response to CpG Motifs in Bacterial DNA					
			and Oligonucleotides, <i>The Journal of Immunology</i> , pp. 558-564 (1996).					
		*C105	Yi, Ae-Kyung et al., Rapid Immune Activation by CpG Motifs in Bacterial DNA, The Journal of					
1			Immunology, pp. 5394-5402 (1996).					
		*C106	Zhao Q et al., Stage-specific oligonucleotide uptake in murine bone marrow B-cell precursors. Blood					
			84(11):3660-6, 1 Dec 1994.					
\Box		*C107	Zhao Q et al., Comparison of cellular binding and uptake of antisense phosphodiester, phosphorothioate, and					
'	•		mixed phosphorothioate and methylphosphonate oligonucleotides. Antisense Res Dev 3(1):53-66, Spring 1993.					
	. 0.	*C108	Liu H-M et al., Immunostimulatory CpG oligodeoxynuçleotides enhance the immune response to vaccine					
¥	/		strategies involving granulocyte-macrophage colony-stimulating factor, <i>Blood</i> 92(10):3730-3736 (1998).					
			2. 10 (1990).					

^{*} a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 09/286/098, filed April 2, 1999, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

EXAMINER (DC)	DATE CONSIDERED /
\mathcal{L}	1 - 1 - 2
Juna	\Q \lambda \text{0} \text{0}

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant